hESC-Derived Motor Neurons For the Treatment of Cervical Spinal Cord Injury

Grant Award Details

hESC-Derived Motor Neurons For the Treatment of Cervical Spinal Cord Injury

Grant Type: Comprehensive Grant

Grant Number: RC1-00345

Investigator:

Name:	Hans Keirstead
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Amyotrophic Lateral Sclerosis, Neurological Disorders, Spinal Cord Injury, Spinal Muscular Atrophy

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,158,445

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: hESC-Derived Motor Neurons For the Treatment of Cervical Spinal Cord Injury

Public Abstract:

Cervical spinal cord injuries result in a loss of upper limb function because the cells within the spinal cord that control upper limb muscles are destroyed. The goal of this research program is to create a renewable human source of these cells, to restore upper limb function in both acute and chronic spinal cord injuries. There are two primary challenges to the realization of this goal: 1) a source of these human cells in high purity, and 2) functional integration of these cells in the body after transplantation.

Human embryonic stem cells (hESCs) can form any cell in the body, and can reproduce themselves almost indefinitely to generate large quantities of human tissue. One of the greatest challenges of hESC research is to find ways to restrict hESCs such that they generate large amounts on only one cell type in high purity such that they could be used to replace lost cells in disease or trauma. Our laboratory was the first laboratory in the world to develop a method to restrict hESCs such that they generate large amounts of only one cell type in high purity. That cell type is called an oligodendrocyte, which insulates connections in the spinal cord to allow them to conduct electricity. Transplantation of these cells was useful for treating spinal cord injuries in rats if the treatment was given one week after the injury. That treatment is being developed for use in humans.

Recent studies in our laboratory indicate that we have succeeded in restricting hESCs to generate large quantities of a different cell type in the spinal cord, that which controls upper limb muscles. We have generated large quantities of these human cells, grown them with human muscle, and demonstrated that they connect and control the human muscle. The cells also express markers that are appropriate for this cell type.

Here we propose to generate these cells in high purity from hESCs and genetically modify them so that they can be induced to grow over inhibitory environments that exist in the injured spinal cord. We will then determine whether these human cells have the ability to regenerate the injured tissue in the spinal cord, and restore lost function. All of our studies will be conducted in an FDA-compliant manner, which will speed the translation of our results to humans if we are successful. The studies outlined in this proposal represent a novel approach to treating spinal cord injury, which might work for both acute and chronic injuries.

Statement of Benefit to California:

This research plan will position California for international competitiveness in this emerging area of biotechnology, as our research strategy addresses critical scientific problems limiting the development of this sector in California and abroad. High purity cultures of hESC-derivatives enable transplantation approaches to disease, drug discovery, and predictive toxicology. This research plan will lead to the development and thorough characterization of a renewable source of human motor neurons that enables these 3 strategies as they pertain to acute spinal cord injury, chronic spinal cord injury, amyotrophic lateral sclerosis, polio, and spinal muscular atrophy. Clinically relevant scientific advance leads to the development of biotechnology companies, creating jobs and taxation. The treatment and care of individuals with disease or trauma-induced disorders of the central nervous system represents a significant economic burden to the State of California. If successful, our research plan will form the basis of a clinical strategy to improve the function and quality of life of spinal cord injured individuals, which may lessen the cost that the State bears in terms of patient care.
